

General Information

CAS Number: 109-09-1
Common Name: 2-Chloropyridine

II. Physical-Chemical Data

A. Melting Point

Test Substance

Identity: 2-Chloropyridine
Remarks: Mean or weighted melting point

Method

Method: Estimation
Remarks: None

Results

Melting Point Value: -12.6°C
Remarks: None

Reference

MPBPWIN v1.40 (EPI Suite™ v.3.10).
Downloadable at
[http://www.epa.gov/oppt/exposure/docs/episuitedl.h](http://www.epa.gov/oppt/exposure/docs/episuitedl.htm)
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Other

B. Boiling Point

Entry 1 of 2

Test Substance

Identity: 2-Chloropyridine
Remarks: None

Method

Method: Estimation
Remarks: Adapted from Stein & Brown method

Results

Boiling Point Value: 150.07°C
Remarks: None

Reference

MPBPWIN v1.40 (EPI Suite™ v.3.10).
Downloadable at
[http://www.epa.gov/oppt/exposure/docs/episuitedl.h](http://www.epa.gov/oppt/exposure/docs/episuitedl.htm)
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Other

Entry 2 of 2 for Boiling Point

Test Substance

Identity:	2-Chloropyridine
Purity:	Not stated
Remarks:	None

Method

Method:	Not stated
GLP:	Not stated
Year:	Not stated
Remarks:	None

Results

Boiling Point Value:	170°C
Remarks:	None

Conclusions

The boiling point was provided in a reliable resource book. The endpoint has been adequately characterized.

Data Quality

Reliability:	2D
Remarks:	Reliable with restrictions; endpoint was provided in a reliable reference text.

Reference

Sax, N. I. and R. J. Lewis, Sr. 1987. Hazardous Chemicals Desk Reference. Pp. 332-333. Van Nostrand Reinhold Co., NY, NY.

Other

C. Vapor Pressure

Test Substance

Identity: 2-Chloropyridine
Remarks: None

Method

Method: Estimation
Remarks: Mean of Antoine and Grain methods

Results

Vapor Pressure Value: 1.56 mmHg @ 25°C
Remarks: None

Reference

MPBPWIN v1.40 (EPI Suite™ v.3.10).
Downloadable at
[http://www.epa.gov/oppt/exposure/docs/episuitedl.h](http://www.epa.gov/oppt/exposure/docs/episuitedl.htm)
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Other

D. Partition Coefficient – Entry 1 of 2

Test Substance

Identity: 2-Chloropyridine
Remarks: None

Method

Method: Estimation
Remarks: None

Results

K_{ow}: 1.45
Remarks: None

Reference

KOWWIN v.1.66. (EPI Suite™ v.3.10).
Downloadable at
[http://www.epa.gov/oppt/exposure/docs/episuitedl.h](http://www.epa.gov/oppt/exposure/docs/episuitedl.htm)
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Other

Entry 2 of 2 for Partition Coefficient

Test Substance

Identity:	2-Chloropyridine
Purity:	Not stated
Remarks:	None

Method

Method:	Not stated
GLP:	Not stated
Year:	Not stated
Remarks:	None

Results

K_{ow} :	1.22
Temperature:	Not stated
Remarks:	None

Conclusions

The partition coefficient was provided in a reliable resource book. The endpoint has been adequately characterized.

Data Quality:

Reliability:	2D
Remarks:	Reliable with restrictions; information provided in a reliable reference text.

Reference

Hansch, C., Leo, A. and Hoekman, D. 1995. Exploring QSAR: Hydrophobic, Electronic and Steric Constants. American Chemical Society. ACS Professional Reference Book, ACS, Washington, DC.

Other

E. Water Solubility

Entry 1 of 2

Test Substance

Identity: 2-Chloropyridine
Remarks: None

Method

Method: Estimation
Remarks: None

Results

Value: 9,609 mg/l
Temperature: 25°C
Remarks: A K_{ow} of 1.22 was used in this estimation.

Reference

WSKOW v1.40 (EPI Suite™ v.3.10).
Downloadable at
[http://www.epa.gov/oppt/exposure/docs/episuitedl.h](http://www.epa.gov/oppt/exposure/docs/episuitedl.htm)
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Other

Entry 2 of 2 for Water Solubility

Test Substance

Identity:	2-Chloropyridine
Purity:	Not stated
Remarks:	None

Method

Method:	Not stated
GLP:	Not stated
Year:	Not stated
Remarks:	None

Results

Value:	2,000 mg/l
Temperature:	25°C
Remarks:	None

Conclusions

The water solubility was provided in a reliable resource book. The endpoint has been adequately characterized.

Data Quality

Reliability:	2D
Remarks:	Reliable with restrictions; information provided in a reliable reference text.

Reference

Lide, D. R. and Frederikse, H. P. R., eds. CRC Handbook of Chemistry and Physics, 75th ed. CRC Press, Boca Raton, FL. 1995.

Other

III. Environmental Fate Endpoints

A. Photodegradation

Test Substance

Identity: 2-Chloropyridine
Remarks: None

Method

Method: Estimation
Test type: Atmospheric oxidation
Remarks: None

Results

Hydroxyl radicals
reaction:
OH Rate
Constant: $0.2603 \times 10^{-12} \text{ cm}^3/\text{molecule-sec}$
Half-life: 41.094 days (12-hr day; $1.5 \times 10^6 \text{ OH/cm}^3$)
Temperature: 25°C
Ozone reaction: No ozone reaction estimation was noted.
Remarks: None

Conclusions

The material is expected to slowly degrade in the atmosphere.

Reference

AopWin v1.90. (EPI Suite™ v.3.10). Downloadable at
<http://www.epa.gov/oppt/exposure/docs/episuiteld.htm>
©2000 U.S. Environmental Protection Agency.

Other

B. Stability in Water

Test Substance

Identity:	2-Chloropyridine
Remarks:	None

The computer modeling program can not estimate the rate constants for aqueous acid/base-catalyzed hydrolysis. Although hydrolysis cannot be predicted using a computer estimation model, 2-chloropyridine does not have a site in which the water molecule or hydroxide ion can displace an atom or group of atoms. Chemical hydrolysis at a pH normally found in the environment, i.e. 5 to 9, can be important for a variety of chemicals that have functional groups that are potentially hydrolysable, such as amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters. It is the position of Arch Chemicals that data for this endpoint is not necessary since this chemical does not possess a structure that is hydrolysable. The judgment is that 2-PCl would be resistant to acid/base-catalyzed hydrolysis.

C. Biodegradation – Entry 1 of 5

Test Substance

Identity: 2-Chloropyridine
Purity: > 96%
Remarks: Purchased from Sigma Chemical Co. St. Louis, MO

Method

Method: Non-specific test method for substrate depletion and methane formation in a sealed system.
Test type: Anaerobic biodegradation in a sediment/water slurry.
GLP: Not stated
Year: 1994
Contact time: 12 months
Inoculum: Sediment and ground water collected from a methanogenic aquifer contaminated with landfill leachate.
Remarks: Experiments were performed in triplicate and employed both sterile and substrate-unamended controls. In addition acetate and 3-chlorobenzene were employed as positive controls. The headspace of the test vessels was monitored for methane formation by gas chromatography (GC). Methane produced in unamended controls was subtracted from that produced in substrate-amended vessels and compared to the theoretically expected amount based on Buswell's equation and the initial substrate concentration. Substrate depletion and metabolite formation was monitored by reverse-phase high-pressure liquid chromatography (HPLC).

Results

Degradation: 2-Chloropyridine was not removed from the test system and evidence of mineralization was not observed.
Results: No methane production was observed. Substrate recovery after 1 year of incubation was $107 \pm 5\%$. No intermediates were observed.
Kinetic: Not stated
Breakdown products: Not stated
Remarks: None

Conclusions

The biodegradability of the test substance has been adequately characterized.

Data Quality

Reliability:

2A

Remarks:

Reliable with restrictions; acceptable, well-documented publication/study report which meets basic scientific principles.

Reference

Adrian, N. R. and Sulfito, J. M. 1994. Anaerobic biodegradation of halogenated and nonhalogenated N-, S- and O-heterocyclic compounds in aquifer slurries. Environ. Toxicol. Chem. 13, 1551-1557.

Other

Entry 2 of 5 for Biodegradation

Test Substance

Identity: 2-Chloropyridine
Purity: Not stated
Remarks: Purchased from Sigma Chemical Co. St. Louis, MO

Method

Method: Non-specific test method for substrate depletion.
Test type: Anaerobic
GLP: Not stated
Year: 1995
Contact time: 12 months
Inoculum: Sediment and ground water collected from a freshwater pond contaminated with small particles of asphalt.
Remarks: Experiments were performed in duplicate and employed both sterile and substrate-unamended controls. Substrate depletion and metabolite formation was monitored by HPLC.

Results

Degradation: 2-Chloropyridine was not removed from the test system.
Results: Some loss of 2-chloropyridine was observed; however, the loss was not significantly different from that in the corresponding sterile controls. No transformation was observed.
Kinetic: Not stated
Breakdown products: Not stated
Remarks: None

Conclusions

The biodegradability of the test substance has been adequately characterized.

Data Quality

Reliability: 2A
Remarks: Reliable with restrictions; acceptable, well-documented publication/study report which meets basic scientific principles.

Reference

Lui, S. M. 1995. Anaerobic dechlorination of chlorinated pyridines in anoxic freshwater sediment slurries. J. Environ. Sci. Health. A30, 485-503.

Other

Entry 3 of 5 for Biodegradation

Test Substance

Identity:	2-Chloropyridine
Purity:	Not stated
Remarks:	Purchased from Aldrich Chemical Co.

Method

Method:	Assessment of degradation based on substrate depletion.
Test type:	Anaerobic biodegradation
GLP:	Not stated
Year:	1989
Contact time:	200 days
Inoculum:	Sediment and overlying site water from an estuary.
Remarks:	Biodegradation of 2-chloropyridine was evaluated in sediment slurries (10% solids) under sulfate reducing conditions. Experiments were replicated and included control sediments. Testing was conducted at 78.8 μ M. Test chambers were incubated in the dark at 23-25°C. Samples for analysis were removed using a syringe and needle periodically. Substrate concentration was measured using HPLC.

Results

Degradation:	None reported
Results:	2-Chloropyridine was persistent in the anoxic sediment.
Kinetic:	Not stated
Breakdown products:	Not stated
Remarks:	None

Conclusions

The biodegradability of the test substance has been adequately characterized.

Data Quality

Reliability:	2B
Remarks:	Reliable with restrictions; basis data given, comparable to guidelines/standards.

Reference

Lui, S. M., Wu, C. H. and Huang, H. J. 1989. Toxicity and anaerobic biodegradability of pyridine and its derivatives under sulfidogenic conditions. Chemosphere 10, 2345-2357.

Other

Entry 4 of 5 for Biodegradation

Test Substance

Identity:	2-Chloropyridine
Purity:	Not stated
Remarks:	None

Method

Method:	Non-guideline specific study of biodegradation of the test substance in soil suspensions.
Test type:	Aerobic biodegradability
GLP:	No
Year:	1986
Contact time:	24 days
Inoculum:	Soil suspension
Remarks:	Degradation experiments were carried out in 500-ml Erlenmeyer flasks. Flasks were prepared to contain 150 ml of basas salts medium amended with yeast extract and potassium phosphate buffer adjusted to pH 7.0. To each replicate flask (note – replication noted in article, but the number of replicates was not specified) 1 ml of 2-chloropyridine solution was added to give a final substrate concentration of approximately 1 mM. Flasks were inoculated with 1 ml of a dilute soil suspension prepared by suspending 15 g soil (Fincastle silt loam) in 1 l of mineral salts medium and continuously stirring while 1-ml aliquots were removed. Flasks were incubated at 24°C for up to 30 days. Subsamples were removed from each flask before and after inoculation and periodically throughout the incubation. 2-Chloropyridine concentrations were monitored by UV spectrophotometry during the incubation period. The disappearance of 2-chloropyridine from solutions plus the mineralization of pyridine-N was taken as evidence of degradation.

Results

Degradation:	UV analysis indicated a 47% loss of 2-chloropyridine from the test solutions by 24 days, while inorganic nitrogen released to the test solutions accounted for <1% degradation.
Results:	2-Chloropyridine did not appear to be appreciable degraded. The amount of 2-chloropyridine lost

from the test solutions determined by UV analysis was 47% within 24 days. Less than 1% was determined to be biodegraded based on release of inorganic nitrogen in the test solutions, while 37% was lost through volatilization and 3.2% adsorbed by soil.

Kinetic: Not stated
Breakdown products: Not stated
Remarks: None

Conclusions

The biodegradability of the test substance has been adequately characterized.

Data Quality

Reliability: 2A
Remarks: Reliable with restrictions; acceptable, well-documented publication/study report which meets basic scientific principles.

Reference

Sims, G. K. and Sommers, L. E. 1986.
Biodegradation of pyridine derivatives in soil suspensions. Environ. Toxicol. Chem. 3, 503-509.

Other

Entry 5 of 5 for Biodegradation

Test Substance

Identity: 2-Chloropyridine
Purity: Not stated
Remarks: None

Method

Method: Non-specific method measuring substance depletion and inorganic N released.
Test type: Aerobic biodegradation in soil
GLP: Not stated
Year: 1985
Contact time: 64 days
Inoculum: The test soil was a Fincast silt loam which had a pH of 6.7, organic carbon content of 12 g/kg, total N content of 1300 mg/kg, CEC of 0.15 mol (+)/kg and contained 0.25 kg H₂O/kg dry soil as – 0.03 MPa.
Remarks: Test chambers were prepared in duplicate and dosed at 200 mmol/kg. At 3- and 4-day intervals the soils were adjusted for loss of moisture. After 0, 1, 2, 4, 8, 16, 32 and 64 days of incubation, the foam stoppers and soil from replicate chambers were extracted and analyzed. In addition, a sterile treatment was extracted and analyzed after 7 days of incubation.

Results

Degradation: 89% of the test substance remained in the soil after 64 days of incubation, indicating little biodegradation of the test substance occurred over the study period. This was confirmed by little inorganic nitrogen accumulation during incubation.
Results: The measured day 0 concentration of the test substance was 113.7% of the nominal concentration. After 64 days of incubation, 89% of the test substance remained in the soil. Accumulation of inorganic nitrogen at days 16, 32 and 64 was equivalent to 1.3, < 0.1 and <0.1% of the extractable test substance.
Kinetic: Not stated
Breakdown products: Not stated
Remarks: None

Conclusions

The biodegradability of the test substance has been adequately characterized.

Data Quality:

Reliability:

2A

Remarks:

Reliable with restrictions; acceptable, well-documented publication/study report which meets basic scientific principles.

Reference

Sims, G. K. and Sommers, L. E. 1985. Degradation of pyridine derivatives in soil: Chemical and biological assessment. J. Environ. Qual. 14, 580-584.

Other

D. Transport between Environmental Compartments (Fugacity)

Test Substance

Identity: 2-Chloropyridine
Remarks: None

Method

Method: Estimation
Model: Level III Fugacity Model
Remarks: None

Results

Estimated distribution and media concentration:		Mass Amount (%)	Half-Life (hr)	Emissions (kg/hr)
	Air	7.52	986	1000
	Water	48.8	900	1000
	Soil	43.6	900	1000
	Sediment	0.104	3.6×10^3	0
Remarks:	Physical chemical values utilized in this model were default values obtained from the EPIWIN program.			

Reference

Level III Fugacity Model. (EPI Suite™ v.3.10).
Downloadable at
<http://www.epa.gov/oppt/exposure/docs/episuitedl.htm>
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Other

IV. Ecotoxicity

A. Acute Toxicity to Fish

Test Substance

Identity: 2-Chloropyridine
Remarks: None

Method

Method: Estimation
Test type: 96-hour LC₅₀
Organism: Fish
Remarks: None

Results

LC₅₀ (96 hours): 277 mg/l
Remarks: None

Reference

Nabholz, J. V., Cash, G., Meylan, W. M. and Howard, P. H. 2001. ECOSAR: A Computer Program for Estimating the Ecotoxicity of Industrial Chemicals Based on Structure Activity Relationships, Version 0.99g. Washington, DC: Risk Assessment Division, Office of Pollution Prevention and Toxics, United States Environmental Protection Agency. Available from EPA web page at <http://www.epa.gov/oppt/newchems/21ecosar.htm> or <http://www.epa.gov/oppt/exposure/docs/episuiteld.htm>

Other

B. Acute Toxicity to Daphnids

Test Substance

Identity: 2-Chloropyridine
Remarks: None

Method

Method: Estimation
Test type: 48-hour LC₅₀
Organism: Daphnid
Remarks: None

Results

LC₅₀ (48 hours): 286 mg/l
Remarks: None

Reference

Nabholz, J. V., Cash, G., Meylan, W. M. and Howard, P. H. 2001. ECOSAR: A Computer Program for Estimating the Ecotoxicity of Industrial Chemicals Based on Structure Activity Relationships, Version 0.99g. Washington, DC: Risk Assessment Division, Office of Pollution Prevention and Toxics, United States Environmental Protection Agency. Available from EPA web page at <http://www.epa.gov/oppt/newchems/21ecosar.htm> or <http://www.epa.gov/oppt/exposure/docs/episuiteld.htm>

Other

C. Acute Toxicity to Aquatic Plants

Test Substance

Identity: 2-Chloropyridine
Remarks: None

Method

Method: Estimation
Test type: 96-hour EC₅₀
Organism: Green Algae
Remarks: None

Results

EC₅₀ (96 hours): 173 mg/l
Remarks: None

Reference

Nabholz, J. V., Cash, G., Meylan, W. M. and Howard, P. H. 2001. ECOSAR: A Computer Program for Estimating the Ecotoxicity of Industrial Chemicals Based on Structure Activity Relationships, Version 0.99g. Washington, DC: Risk Assessment Division, Office of Pollution Prevention and Toxics, United States Environmental Protection Agency. Available from EPA web page at <http://www.epa.gov/oppt/newchems/21ecosar.htm> or <http://www.epa.gov/oppt/exposure/docs/episuiteld.htm>

Other

V. Mammalian Toxicity

A. Acute Toxicity – Entry 1 of 5

Test Substance

Identity: 2-Chloropyridine
Purity: Not determined
Remarks: None

Method

Method: Not stated
Type: LD₅₀
GLP: No
Year: 1964
Species/Strain: Rat/Manor Wistar
Sex: Male
Number of animals/
sex/dose: 6
Vehicle: Methylcellulose
Route of
administration: Oral (gavage)
Remarks: Groups of 6 male rats were administered a single dose of the test substance suspended in a 0.5% aqueous dispersion of methylcellulose via oral gavage at concentrations of 100, 215, 464, 681, 1000, 1470 and 2150 mg/kg. Each dose level was prepared in a concentration that enabled the delivery of a constant volume of 1.0 ml/100 g of body weight. Rats were in the weight range of 201-304 g. Food was withheld from all rats for 16 hours prior to dosing. Food and water were available *ad libitum* at all other times. Rats were observed for signs of toxicity and mortality continuously for 4 hours post-dose, at 24 hours post dose and once daily thereafter for 13 days. At the termination of the 14-day observation period, surviving rats were sacrificed. Necropsies were performed on all rats.

Results

Value: LD₅₀ – 342 mg/kg (confidence limits – 211 – 558 mg/kg)

Mortality rate:	Dose (mg/kg)	Mortality
	100	0/6
	215	1/6
	464	5/6
	681	6/6
	1000	6/6

1470	6/6
2150	6/6

Remarks:

At 16 hours post-dose, 4 rats in the 100 mg/kg dose group exhibited nasal porphyrin. At 24 hours post-dose, 4 rats appeared hypoactive. All animals appeared normal thereafter until study termination. Two rats in the 215 mg/kg dose group exhibited nasal porphyrin discharge at 4 hours post-dose. At 24 hours post-dose 4 rats were ataxic, sedate, hypoactive and displayed nasal porphyrin discharge. At 2 days all rats were hypoactive and continued to demonstrate nasal discharge. One animal was found dead on day 3. The remaining rats appeared normal throughout the remainder of the observation period. Within 6 hours 5 rats from the 464 mg/kg dose group exhibited ataxia and hypoactivity. One rat became prostrate. At 24 hours all rats were ataxic and exhibited nasal porphyrin. One rat was prostrate and dyspneic. At 2 days 1 rat died and 2 were ataxic and the remaining 3 appeared hypoactive. At 3 days all 5 rats were hypoactive and appeared depressed. At 4 days one died and the remaining 4 continued to be hypoactive and became hypersensitive to touch. Two more rats died on days 5 and 6. The remaining 2 rats were hypoactive and hypersensitive to touch. A fifth rat died. The remaining rat recovered and appeared normal from days 9 through 14. rats in the 681, 1000, 1470 and 2150 mg/kg dose groups displayed hypotonia, ataxia, sedation, hypnosis, loss of righting reflex, pinna and placing reflexes, bradypnea, dyspnea, cyanosis, ptosis, salivation and reduced pain responses within 2 to 18 hours post-dose. Rats in all dose groups except the 681 mg/kg dose group died within 2 to 4 hours post-dose. Rats in the 681 mg/kg dose group died within 3 days. At necropsy, 1 rat in the 100 mg/kg dose group had hydronephrosis. The rat that died in the 215 mg/kg dose group exhibited a pale liver with friable accentuated lobules and the lungs were congested. Necropsy findings in the rats that died in the 464 mg/kg dose group included congested lungs, congested liver, hemorrhages of the stomach, small intestines and urinary bladder and icterus. All rats in the 100, 215 and 464 mg/kg dose groups that

survived to the 14-day post-exposure period had essentially normal necropsy findings. Necropsy findings in the 681, 1000, 1470 and 2150 mg/kg dose groups included scrotal erythema, hemorrhages of the stomach, intestines and urinary bladder and congested lungs and liver. Hydronephrosis (unilateral and bilateral) was scattered in all groups.

Conclusions

Remarks:

The acute oral LD₅₀ has been adequately characterized.

Data Quality

Reliability:

1B

Remarks:

Reliable without restriction; comparable to guideline study.

Reference

Wazeter, F. X. 1964. Acute Toxicity Studies in Rats and Rabbits. Report # 122-003. International Research and Development Corporation, Mattawan, MI.

Other

Acute Toxicity – Entry 2 of 5

Test Substance

Identity: 2-Chloropyridine
Purity: > 97%
Remarks: None

Method

Method: “Sleeve” technique described by Draize et al. (1944) and Rowe et al. (1952). These references are cited in the study reference.
Type: LD₅₀
GLP: No
Year: 1966
Species/Strain: Rabbit
Sex: Male and female
Number of animals/dose: 4-5
Vehicle: None
Route of administration: Dermal
Remarks: Groups of male and female rabbits, weighing 1.3 to 2.3 kg, were exposed to the undiluted test substance dermally at concentrations of 40, 48, 50, 58, 63, 68, 79, 82 or 100 mg/kg.

Results

Value: LD₅₀ – 64 mg/kg (confidence limits – 55.5 to 73.5 mg/kg)

Mortality rate:	Dose (mg/kg)	Mortality
	40	0/5
	48	1/4
	50	1/5
	58	2/5
	63	3/4
	68	2/5
	79	3/4
	82	3/5
	100	5/5

Remarks: The test substance caused only transient local congestion of the skin when applied to either intact or abraded skin. The primary gross lesion observed was hemorrhagic necrosis of the liver.

Conclusions

Remarks: The acute dermal LD₅₀ has been adequately characterized.

Data Quality

Reliability: 2A
Remarks: Reliable with restriction; acceptable, well-documented publication which meets basic scientific principles.

Reference

Gehring, P. J., Torkelson, T. R. and Oyen, F. 1967. A Comparison of the Lethality of Chlorinated Pyridines and a Study of the Acute Toxicity of 2-Chloropyridine. Toxicol. Appl. Pharmacol. 11, 361-371.

Other

Acute Toxicity – Entry 3 of 5

Test Substance

Identity:	2-Chloropyridine
Purity:	Not determined
Remarks:	None

Method

Method:	Not stated
Type:	Acute dermal toxicity
GLP:	No
Year:	1964
Species/Strain:	Rabbit
Sex:	Male and female
Number of animals/ sex/dose:	3
Vehicle:	None
Route of administration:	Dermal
Remarks:	Six rabbits (3 M; 3 F) per group, weighing between 2040 and 2828 g, were administered a single dose of the undiluted test substance dermally at concentrations of 200 and 2000 mg/kg. The back of each rabbit was clipped. The clipped back of 3 rabbits per group was abraded and the skin of the remaining 3 rabbits was left intact. The rabbits were exposed to the test substance for a period of 24 hours. The dosing site was not occluded during the 24 hour exposure period. Rabbits were observed frequently for pharmacotoxic effects during the first 4 hours after application, at 24 hours and once daily thereafter for a total of 14 days. The degree of dermal irritation and damage was evaluated. At the end of the observation period all surviving rabbits were weighed, sacrificed and necropsied. Rabbits that did not survive the observation period also were necropsied.

Results

Value:	LD ₅₀ – < 200 mg/kg
Mortality rate:	200 mg/kg – 5/6 2000 mg/kg – 6/6

Remarks:	Five rabbits in the 200 mg/kg dose group died within 18 to 40 hours post-dose. Death was preceded by cyanosis, bradypnea and dyspnea,
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lacrimation, hypothermia and hypotonia of the skeletal musculature. One rabbit with intact skin survived. This rabbit demonstrated a very slight erythema of the area of application for the entire observation period. All rabbits in the 2000 mg/kg dose group died within 18 hours after displaying signs as noted above. Necropsy findings in the 200 mg/kg dose group included excessive mucous in the stomach and lungs that failed to collapse and which were congested and hemorrhagic. Fluid was found in the thoracic cavity and a strong odor of the test substance was present in the thoracic cavity. One rabbit displayed a hemorrhagic cecum. The surviving rabbit in this group exhibited no gross lesions. Necropsy findings in the 2000 mg/kg dose group included excessive mucous in the stomach and lungs that failed to collapse and which were congested and hemorrhagic. Foam was present in the trachea and major bronchi. A strong test substance odor was present in the thoracic cavity of all rabbits.

Conclusions

Remarks:

The acute dermal toxicity has been adequately characterized.

Data Quality

Reliability:

1B

Remarks:

Reliable without restriction; comparable to guideline study.

Reference

Wazeter, F. X. 1964. Acute Toxicity Studies in Rats and Rabbits. Report # 122-003. International Research and Development Corporation, Mattawan, MI.

Other

Acute Toxicity – Entry 4 of 5

Test Substance

Identity:	2-Chloropyridine
Purity:	> 97%
Remarks:	None

Method

Method:	Not stated
Type:	Acute inhalation toxicity
GLP:	No
Year:	1966
Species/Strain:	Rat
Sex:	Female
Number of animals/ dose:	10-20
Vehicle:	None
Route of administration:	Inhalation
Remarks:	<p>Groups of female rats, approximately 10 weeks old and weighing 132 to 190 g, were exposed to the test substance via inhalation at concentrations of 50, 100, 250, 500 and 1000 ppm for 0.1 to 7.0 hours. The concentration of 2-chloropyridine was monitored continuously during the exposure by infrared spectrophotometry. The degree and character of organic damage resulting from exposure to the test substance were the presence of gross pathologic or histopathologic lesions, hematologic alterations, organ weight changes and changes in the blood chemistry. Liver, kidney, spleen, heart, lungs and brain were examined for weight changes and together with pancreas and adrenals for the presence of histologic lesions. Hematologic studies consisted of erythrocyte, leukocyte and differential counts and hematocrit and hemoglobin determinations. Parameters used to detect changes in blood chemistry were blood urea nitrogen, serum glutamic-pyruvic transaminase and serum glutamic-oxalacetic transaminase. Rats were observed for 2 weeks post-exposure.</p>

Results

Value:	LC ₅₀ – > 100 ppm but < 250 ppm
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Mortality rate:	Dose Level (ppm)	Length of Exposure (hrs)	Mortality Rate
	50	7.0	0/10
		4.0	0/10
	100	7.0	13/20
		4.0	7/20
		2.0	0/10
	250	7.0	12/12
		4.0	14/20
		2.0	8/10
		1.0	2/10
		0.5	0/10
	500	2.0	15/15
		1.0	8/15
		0.5	2/15
		0.2	0/14
	1000	1.0	14/15
		0.5	8/10
		0.2	8/17
		0.1	0/20

Remarks: The concentration of 2-chloropyridine vapor was within 7% of the desired concentration throughout the exposure period. Liver damage was the primary alteration caused by the inhalation of the test article. Histopathologic examinations revealed that the test substance caused central lobular necrosis, hemorrhage and fatty degeneration as well as cellular infiltration. The extent and type of damage varied with the exposure. Maximum single-dose exposures not causing these changes were 100 ppm for 3 minutes, 50 ppm for 6 minutes, 25 ppm for 12 minutes and 10 ppm for 30 minutes. Maximum single-dose exposures that did not cause death 1000 ppm for 6 minutes, 500 ppm for 12 minutes, 250 ppm for 30 minutes, 100 ppm for 2 hours and 50 ppm for 4 hours.

Conclusions

Remarks: The LC₅₀ was not calculated, but based on the available data, the 4-hour LC₅₀ is between 100 and

250 ppm. Therefore, the acute inhalation LC₅₀ has been adequately characterized.

Data Quality

Reliability:

2A

Remarks:

Reliable with restriction; acceptable, well-documented publication which meets basic scientific principles.

Reference

Gehring, P. J., Torkelson, T. R. and Oyen, F. 1967. A Comparison of the Lethality of Chlorinated Pyridines and a Study of the Acute Toxicity of 2-Chloropyridine. Toxicol. Appl. Pharmacol. 11, 361-371.

Other

Acute Toxicity – Entry 5 of 5

Test Substance

Identity:	2-Chloropyridine
Purity:	Not determined
Remarks:	None

Method

Method:	Not stated
Type:	Acute inhalation toxicity
GLP:	No
Year:	1964
Species/Strain:	Rat
Sex:	Male
Number of animals/ sex/dose:	10
Vehicle:	None
Route of administration:	Inhalation
Remarks:	Ten male albino rats, weighing 235 to 270 g, were exposed to the test substance via inhalation at a concentration of approximately 6.05 mg/l for 6 hours. The exposure was conducted in a 354 l stainless steel chamber. The total airflow through the system was 49±1 liters/minute. Food and water were available <i>ad libitum</i> , except during the period of exposure. During exposure, rats were observed for signs of toxicity and mortality continuously for 1 hour and at ½ hour intervals thereafter until the end of the exposure period. After the exposure period, the rats were observed daily for 14 days. A necropsy was performed on all rats.

Results

Value:	LC ₅₀ – < 6.05 mg/l
Mortality rate:	10/10
Remarks:	All animals died within 3 days after exposure. Observations during exposure included hypoactivity, sedation and ataxia. At the end of 4 hours of exposure, all rats were prostrate. Three rats exhibited dyspnea. Three rats died between 4 and 6 hours of the exposure period. At the end of 6 hours the surviving rats were prostrate, comatose and dyspneic. Within 24 hours, 2 additional rats died. The remaining 5 rats were still prostrate and comatose. Clear ocular discharge was noted.

Within the following 24- hour period after exposure, 4 more rats died. The tenth rat died at 3 days post exposure. Necropsy findings in all rats included congestion of the lungs and liver, slight congestion of the small intestines, blood in the abdominal cavity and /or severe hemorrhages of the stomach, small intestines and urinary bladder.

Conclusions

Remarks:

The acute inhalation toxicity has been partially characterized. These data support the data of Gehring et al. (1967).

Data Quality

Reliability:

1B

Remarks:

Reliable without restriction; comparable to guideline study.

Reference

Wazeter, F. X. 1964. Acute Toxicity Studies in Rats and Rabbits. Report # 122-003. International Research and Development Corporation, Mattawan, MI.

Other

B. Genetic Toxicity *In Vitro*– Entry 1 of 3

Test Substance

Identity:	2-Chloropyridine
Purity:	99%
Remarks:	None

Method

Method:	Ames/ <i>Salmonella</i> Bacterial Point Mutation Assay
Type:	Reverse mutation assay
Test system:	Bacteria
GLP:	Not stated
Year:	1987
Species/Strain:	<i>Salmonella typhimurium</i> /TA97, TA98, TA100 and TA102
Metabolic activation:	9000 g (S9) liver homogenate from Arochlor 1254-induced male Sprague-Dawley rats.
Concentrations tested:	50, 100, 500, 1000 and 5000 µg/plate without S9 50, 100, 500, 1000, 5000 and 7500 µg/plate with S9
Statistical methods:	Stead et al. (1981) and Bernstein et al. (1982) from the reference list in the cited study.
Remarks:	The test procedures were the same as initially described by Ames et al. (1975) (in reference list of cited study). All assays were conducted in the standard plate incorporation assay on at least 2 separate days both with and without metabolic activation. The test substance was tested at 6 concentrations in duplicate. Appropriate negative (solvent) and positive controls were run in parallel with the assay. The test substance and solvent control were dissolved in dimethyl sulfoxide (DMSO). The test substance was not designated positive or negative unless reproducible results were obtained. A positive response was defined as a reproducible, concentration-related increase in histidine independent revertants over the solvent control concentration in at least one strain/activation combination. A definitive positive or negative result was assigned to a test result when the statistical methods and visual examination of the data agreed. An equivocal response occurred when 1) test results were not reproducible, 2) a low-level, but not concentration-related, increase in <i>his</i> + colonies was obtained or 3) when an increase was observed at only 1 concentration level.

Results

Result: 2-Chloropyridine elicited a mutagenic response in all 4 *Salmonella* strains in the presence of the metabolic activation system only. No toxicity was observed at any concentration.

Cytotoxic
Concentration: None

Genotoxic effects: Negative without metabolic activation. Positive with metabolic activation in all tester strains.

Statistical results: Not stated

Remarks: None

Conclusions

Remarks: This endpoint has been adequately characterized.

Data Quality

Reliability: 1B

Remarks: Reliable without restriction; comparable to guideline study.

Reference

Claxton, L. D., Dearfield, K. L., Spanggord, R. J., Riccio, E. S. and Mortelmans, K. 1987. Comparative mutagenicity of halogenated pyridines in the *Salmonella typhimurium*/mammalian microsome test. *Mutat. Res.* 176, 185-198.

Other

Genetic Toxicity *In Vitro*– Entry 2 of 3

Test Substance

Identity: 2-Chloropyridine
Purity: Not stated
Remarks: None

Method

Method: Not stated
Type: Mammalian cell forward mutation assay
Test system: Mammalian cells
GLP: Not stated
Year: 1992
Cell type: Heterozygous L5178Y TK^{+/−} -3.7.2C mouse lymphoma cells.
Metabolic activation: S9 homogenate derived from livers of Arochlor-induced rats.
Concentrations tested: Ranging from 1200-2004 µg/ml without S9 activation.
Ranging from 400-1100 µg/ml with S9 activation
Statistical methods: Not stated
Remarks: Duplicate cultures of L5178/TK^{+/−} -3.7.2C cells were treated with or without metabolic activation for 4 hours according to the procedures described by Turner et al. (1984)(in reference list of cited study). The mutagenicity assay was performed according to the procedures described by Doerr et al. (1989) (in reference list of cited study). A positive response was defined as one in which the induced mutant frequency was $>70 \times 10^{-6}$, at concentrations yielding $>10\%$ relative total growth. Equivocal responses were those that gave approximately equal evidence of positive and negative responses. The positive control compounds were ethyl methanesulfonate (without S9) and benzo[a]pyrene (with S9).

Results

Result: In the absence of metabolic activation, 2-chloropyridine induced small increases in the mutant frequencies. In the presence of the metabolic activation system, the test substance greatly increased the frequency of gene mutations.

The test substance induced both small and large colony tk mutants.

Cytotoxic

Concentration: None

Genotoxic effects: Positive

Statistical results: Not stated

Remarks: An analysis of the relative small and large colony tk mutant frequencies was not performed because the induced response was not sufficient to allow interpretation of the data. Colony sizing was performed on the positive control cultures. Colony sizing analysis for the positive controls demonstrated the ability to recover and quantitate both classes of tk mutants.

Conclusions

Remarks: This endpoint has been adequately characterized.

Data Quality

Reliability: 2A

Remarks: Reliable with restriction; acceptable, well-documented publication which meets basic scientific principles.

Reference

Dearfield, K. L., Harington-Brock, D., Doerr, D. L., Parker, L. and Moore, M. M. 1993. Genotoxicity of three pyridine compounds to L5178Y mouse lymphoma cells. *Mutat. Res.* 301, 57-63.

Other

Genetic Toxicity *In Vitro*– Entry 3 of 3

Test Substance

Identity: 2-Chloropyridine
Purity: Not stated
Remarks: None

Method

Method: Not stated
Type: Mammalian cell chromosome aberrations and micronuclei
Test system: Mammalian cells
GLP: Not stated
Year: 1992
Cell type: Heterozygous L5178Y TK^{+/+}-3.7.2C mouse lymphoma cells.
Metabolic activation: S9 homogenate derived from livers of Arochlor-induced rats.
Concentrations tested: Ranging from 1920-1992 µg/ml without S9 activation.
Ranging from 500-1100 µg/ml with S9 activation
Statistical methods: Not stated
Remarks: Duplicate cultures of L5178/TK^{+/+}-3.7.2C cells were treated with or without metabolic activation for 4 hours according to the procedures described by Turner et al. (1984)(in reference list of cited study). The cytogenetic analysis was performed according to the procedures described by Doerr et al. (1989) (in reference list of cited study). For the cytogenetic endpoints a positive call is based upon meeting 2 criteria: The response was double the negative control for not only the experiment but also the periodically updated historic means for negative controls. Positive control cultures were analyzed for cytogenetic endpoints only for those compounds that demonstrated a very weak or equivocal response in the mutagenesis assay. The positive control compound was ethyl methanesulfonate (without S9).

Results

Result: In the absence of metabolic activation, the test substance induced a small increase in the frequency of chromosome aberrations. In the presence of metabolic activation, it significantly increased the frequency of chromosome aberrations. The test substance significantly increased the number of micronuclei with and without metabolic activation.

Cytotoxic

Concentration: None

Genotoxic effects: Positive

Statistical results: Not stated

Remarks: An analysis of the relative small and large colony tk mutant frequencies was not performed because the induced response was not sufficient to allow interpretation of the data. Colony sizing was performed on the positive control cultures. Colony sizing analysis for the positive controls demonstrated the ability to recover and quantitate both classes of tk mutants.

Conclusions

Remarks: This endpoint has been adequately characterized.

Data Quality

Reliability: 2A

Remarks: Reliable with restriction; acceptable, well-documented publication which meets basic scientific principles.

Reference

Dearfield, K. L., Harington-Brock, D., Doerr, D. L., Parker, L. and Moore, M. M. 1993. Genotoxicity of three pyridine compounds to L5178Y mouse lymphoma cells. *Mutat. Res.* 301, 57-63.

Other